



4. (Cancelled)

5. (Original) The process according to claim 1, in which said hexamethyldisilazane metal salt is a hexamethyldisilazane alkali metal salt.

6. (Original) A process according to claim 5, in which said hexamethyldisilazane metal salt is chosen from the hexamethyldisilazane lithium salt, the hexamethyldisilazane sodium salt, and the hexamethyldisilazane potassium salt.

7. (Original) The process according to claim 6, in which said hexamethyldisilazane metal salt is used in an amount ranging from 20 to 30 molar equivalents.

8. (Previously Presented) The process according to claim 1, in which, when the treatment of the cyclosporin is carried out in the presence of a metal halide, said metal halide is chosen from lithium chloride, caesium chloride, caesium fluoride, cuprous chloride, and mercuric chloride.

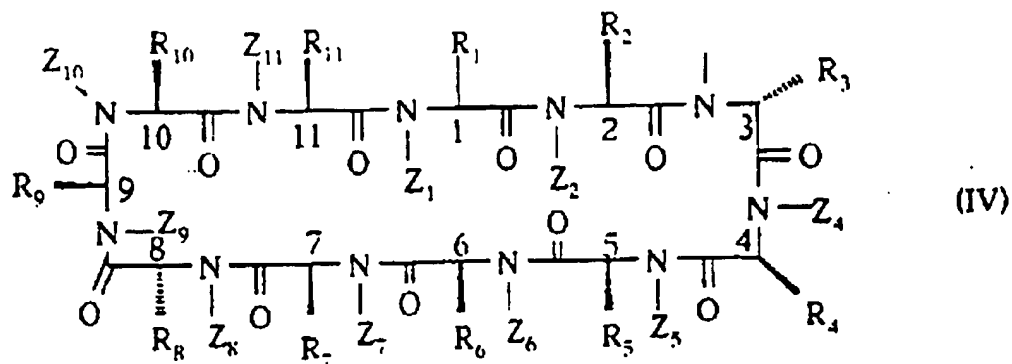
9. (Original) The process according to claim 8, in which, when said metal halide is caesium chloride or lithium chloride, it is used in an amount ranging from 2 to 8 molar equivalents.

10. (Original) The process according to claim 9, in which the treatment of the cyclosporin is carried out in an aliphatic or cyclic ether, an aromatic hydrocarbon, or a mixture of these solvents.

11. (Original) The process according to claim 10, in which the treatment of the cyclosporin is carried out at a temperature ranging from -40°C to 0°C.

12. (Original) The process according to claim 11, in which the treatment of the cyclosporin is carried out with a ratio (weight/weight) of cyclosporin involved with respect to the total weight of the solution which is less than or equal to 10%.

13. (Currently Amended) A process for preparing a cyclosporin derivative substituted at the 3-position, said process comprising preparing a polyanion by treating a cyclosporin with a hexamethyldisilazane metal salt, optionally in the presence of a metal halide, adding an electrophilic agent to said treated cyclosporin, and, optionally converting the product of said addition to a salt, in which at least one obtained cyclosporin derivative substituted at the 3-position has the formula:



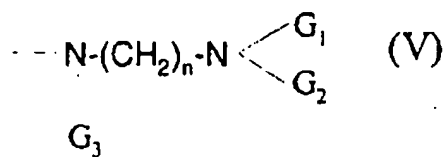
in which

the radicals  $R_1$ ,  $R_2$ , and  $R_4$  to  $R_{11}$ , and  $Z_1$ ,  $Z_2$ , and  $Z_4$  to  $Z_{11}$  are defined as for cyclosporin A, with the exception of  $R_4$  and  $Z_4$ , which are defined so as to have, at the 4-position, the amino acid 4'-hydroxy-methyllucine, and of  $R_3$ , which is  $-S-CH_3$  or a radical  $-S-Alk-R^\circ$  in which:

Alk is an alkylene radical comprising from 2 to 6 straight- or branched-chain carbon atoms or a cycloalkylene radical comprising from 3 to 6 carbon atoms;  
and

$R^\circ$  is

a hydroxyl, carboxyl, or alkyloxycarbonyl radical; or  
an  $-NG_1G_2$  radical or a radical of formula:



in which G<sub>1</sub> and G<sub>2</sub>, which are identical or different, are each a hydrogen atom; or

a phenyl, cycloalkyl (C<sub>3-6</sub>), alkenyl (C<sub>2-4</sub>), or alkyl radical, each of which is optionally substituted by a halogen atom, an alkyloxy, alkyloxycarbonyl, amino, alkylamino, or dialkylamino radical; or

a benzyl radical or a saturated or unsaturated heterocyclyl radical comprising 5 or 6 ring members and from 1 to 3 heteroatoms; or

G<sub>1</sub> and G<sub>2</sub> form, with the nitrogen atom to which they are attached, a saturated or unsaturated heterocycle comprising from 4 to 6 ring members which can comprise another heteroatom chosen from nitrogen, oxygen, and sulphur and which is optionally substituted by alkyl, phenyl, or benzyl; and

G<sub>3</sub> is a hydrogen atom or an alkyl radical, and n is an integer from 2 to 4, the alkyl portions or radicals defined above are straight or branched and comprise from 1 to 4 carbon atoms.

14. (Cancelled)

15. (Withdrawn) A method for preventing or treating a retrovirus infection or an associated syndrome, comprising administering to a mammal in need or desire thereof an effective amount of a cyclosporin derivative as defined in claim 14 in 1), 2), 3), 4), or 7).

16. (Withdrawn) The method of claim 15, in which the retrovirus infection is AIDS (acquired immunodeficiency syndrome).

17. (Withdrawn) A method for treating a chronic inflammatory disease or an autoimmune disease, comprising administering to a mammal in need or desire thereof an effective amount of a cyclosporin derivative as defined in claim 14 in 5).

18. (Withdrawn) A method for preventing or treating an autoimmune disease or preventing rejection of a transplanted organ, comprising administering to a mammal in need or desire thereof an effective amount of a cyclosporin derivative as defined in claim 14 in 6) or 8).

19. (Withdrawn) A method for treating inflammation, comprising administering to a mammal in need or desire thereof an effective amount of a cyclosporin derivative as defined in claim 14 in 6) or 8).

20. (Withdrawn) The method of claim 19, in which the inflammation is an arthritis or a rheumatic disease.

21. (Withdrawn) A method for treating schistosomiasis, filariasis, leishmaniasis, coccidioidomycosis, or malaria, comprising administering to a mammal in need or desire thereof an effective amount of a cyclosporin derivative as defined in claim 14 in 6) or 8).

22. (Cancelled)

23. (Previously Presented) The process according to claim 13, wherein said cyclosporin derivative substituted at the 3-position is [(R)-2-(N,N-dimethylamino)ethylthio-Sar]<sup>3</sup>-[4'-hydroxy-MeLeu]<sup>4</sup>-cyclosporin A.

24. (Previously Presented) The process of claim 13, in which at least one hydroxyl radical present on said cyclosporin that interferes with the treating reaction is protected before said treatment with a protective radical and then the protective radicals are removed after said treatment.